What's New in Pediatrics

Rheumatic Fever

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THE seriousness of the rheumatic fever problem has at long last been recognized. Public-spirited organizations and the medical profession have joined hands in a concerted effort to procure funds for research and for the dissemination of the knowledge already accumulated on the symptomatology, diagnosis and treatment of rheumatic fever. In 1948 there were 22 state and 22 private rheumatic fever programs.

Angove[1] reported that rheumatic fever kills more than five times as many persons annually as poliomyelitis, pertussis, diphtheria, scarlet fever, measles and meningitis combined. For every case of poliomyelitis in the age group 5 to 15 years there are 111 cases of rheumatic fever, and for every death from poliomyelitis there are 154 deaths from rheumatic fever.

Martin[10] has estimated that each year 40,000 persons die from rheumatic fever and its sequelae in the United States, and that between 800,000 and 1,000,000 new cases develop annually. Rheumatic fever ranks first as a cause of death for girls in New York City and is second only to accidents for boys.

Meakins[12] found the disease seven times more common in urban than in rural school populations. The disease is about 20 times more common in the working class than among the wealthy. There is a pronounced seasonal variation coinciding with the prevalence of hemolytic streptococcus infections. At one time it was felt that rheumatic fever was a disease of the temperate zone. We now know it has a universal distribution, but occurs less commonly and is generally less virulent in subtropical and tropical areas where streptococcal infections are not as prevalent. Clark[3] observed no cases of mitral stenosis during 30 years in the tropics. He found 747 cases of joint involvement and other manifestations, obviously rheumatic, but no rheumatic heart disease. These data were gathered from observation of 571,526 clinic outpatients drawn from an estimated population of 33,748,369.

Coburn and Moore[4] have expressed the opinion that there are three factors in the genesis of the rheumatic state:

1. A constitutional factor transmitted as a single autosomal recessive gene—a conclusion reached by Wilson and Schweitzer[22] based on the quantitative agreement between the observed incidence and the value predicted from this hypothesis. The presence of this recessive gene alters the host in some manner as yet unknown, to make him constitutionally susceptible. It has been estimated that about 5 per cent of the population are so affected. The onset of rheumatic fever in this susceptible 5 per cent of the population depends on the two other factors, namely:

2. Infection with the hemolytic streptococcus, whose products precipitate the rheumatic attack, and

3. Deficiency in the host of certain dietary factors.

Cavelte[2] has recently carried out some interesting experimental studies supporting the generally accepted belief that the rheumatic process is initiated by the hemolytic streptococcus. He found that nonantigenic emulsions of homologous heart muscle and connective tissue can be rendered antigenic for rabbits by combining them with heat-killed hemolytic streptococci. Such a mixture when injected into rabbits produced valvular endocarditis with inflammatory infiltration and proliferation. Mixtures of skeletal muscle, free from connective tissue, and hemolytic streptococci did not produce cardiac lesions. Cavelte found antibodies to human heart in titers of 1:40 to 1:320 in 47 out of 67 samples tested from patients with rheumatic heart disease. On the basis of these studies Kerr[9] suggested that the hemolytic streptococci or their products, in conjunction with the connective tissues of the body, produce auto-antibodies which are the cause of the lesions associated with the rheumatic state. Previously, Rich and Gregory[15] produced lesions in laboratory animals similar to those of rheumatic carditis by inducing anaphylactic hypersensitivity to sulfonamides. They later produced widespread vascular lesions similar to rheumatic arteritis, lupus erythematosus and periarteritis nodosa by anaphylactic hypersensitivity. These studies are additional evidence supporting the role of the factor of hypersensitivity in rheumatic fever.

The importance of the diet in the pathogenesis of rheumatic fever is not clearly understood. Coburn and Moore[4] found that children with recrudescences were lacking in proteins, iron, vitamin A and possibly calcium and riboflavin.

Jackson and co-workers,[8] from a study of rheumatic subjects receiving supervised diets and environmental care, concluded that if the disease is definitely inactive, adequate diet and good care will practically eliminate the chances of recurrence with

Presented as part of a Panel Discussion on What's New in Pediatrics before the Section on Pediatrics at the 78th Annual Meeting of the California Medical Association, May 8-11, 1949, Los Angeles.

carditis. They found that the degree of deficiency of the diet was related to the incidence and degree of cardiac damage.

Van Breeman, cited by Coburn and Moore,[4] reported that in the Netherlands there were only 228 deaths from rheumatic fever between the years 1920 and 1925. In the industrial cities of England it was a very important cause of death. The climate, race, age and incidence of respiratory infections were about the same in the two countries. The major difference was in the diet, the people of the Netherlands receiving abundant amounts of dairy products. The role of the diet is difficult to evaluate, however, as the increased incidence of rheumatic fever in the group on an inadequate diet may be due to an increased susceptibility to infections.

Griffith[6] has divided the rheumatic cycle into four phases:

1. The phase during which the patient is host to the hemolytic streptococcus. Swift[18] is of the opinions that if all cases of rheumatic fever could be studied bacteriologically and immunologically for the presence of antibodies against streptococcal components, practically all would be shown to have a "Phase 1" prior to the attack of rheumatic fever. The site of the infection is generally believed to be in the upper respiratory tract and the offending substance is probably produced locally.

2. The latent phase which lasts from one to four weeks. This is one of the most characteristic features of this disease. It is during this period that the immunologic reactions are becoming established.

3. The period of rheumatic activity during which the classical symptoms of rheumatic fever occur, and

4. The period of rheumatic inactivity. The fourth period may be the end to the rheumatic process or may be followed by one or more recurrences.

Much emphasis has been put on the major and minor criteria of rheumatic fever in recent years. Although there have been minor differences of opinion, the consensus is that carditis, subcutaneous nodules, erythema marginatum, polyarthritis, chorea and a history of a preceding attack are the major criteria. Fever, abdominal pain, precordial pain, non-traumatic epistaxis, weight loss, tachycardia and pneumonitis are listed as the important minor criteria.

Such a division of symptoms is of value in bringing to mind the important features of the disease. It is not without danger, however, to dictate strict standards of diagnosis which depend on a specific number of major and minor criteria being present. The ability to evaluate the material at hand comes only after years of intimate contact with rheumatic patients. One need only to make rounds on any rheumatic fever service or attend any cardiac clinic to realize, from the differences of opinion expressed by those who helped formulate the criteria, that such a punch-board method will never work in the diagnosis of rheumatic fever any more than it has worked in the diagnosis of any other disease. The major and minor criteria are aids in diagnosis, nothing more.

The electrocardiogram, erythrocyte sedimentation rate and x-ray remain the chief laboratory procedures used in the appraisal of the child suspected of having rheumatic fever and in directing therapy during the period of activity. The most frequent changes in the electrocardiogram are an increase in the PR interval, changes in the QRST or ventricular portion of the electrocardiogram, and disturbances of rhythm. Frequently repeated electrocardiograms are important in the proper evaluation of any deviation from normal. A change in the electrocardiogram during the period of observation is more important in indicating rheumatic activity than the existence of any specific variation from the accepted normal.

Recently Taran[19, 20, 21] has emphasized the importance of the Q-T quotient as an indication of rheumatic activity. The Q-T interval is the duration of electrical systole, and its use as an indication of cardiac function is based on the physiological principle that a disturbance in the time relationship of systole and diastole is a manifestation of impairment of the functional integrity of the myocardium. When electrical systole is prolonged the diastolic period or perfusion time of the heart muscle is shortened. This results in local tissue anoxia and ultimate heart failure.

The erythrocyte sedimentation rate should be used with caution in the diagnosis of rheumatic fever. There is a tendency to attribute undue importance to this laboratory procedure. It should be evaluated in the light of the history, physical findings and other laboratory data. It is more useful and more reliable as a guide in the management of the rheumatic patient, but even here it is sometimes misleading in either direction.

An x-ray of the chest for heart size is valuable as a base line for future comparison. Schwedel[17] has expressed the belief that progressive cardiac enlargement or the enlargement of an individual cardiac chamber as compared to a previous film is an indication of rheumatic activity. The chambers most commonly enlarged are the left auricle and the right auricle and ventricle. Pulmonary complications and pancarditis are not uncommonly encountered and roentgen study then is needed for confirmation of the clinical impression. It must again be emphasized that this is just another aid in the diagnosis and treatment and should not in any way supplant a careful history, detailed physical examination and the other laboratory procedures of value in the appraisal of the child with rheumatic fever.

MANAGEMENT

Bed rest continues to be the cornerstone in the management of the child with rheumatic fever. It is unfair to follow any set rule for the period of complete bed rest. Each case should be judged

individually. But bed rest should by all means be continued until all signs of activity as manifested by fever, sleeping pulse rate, electrocardiogram and sedimentation rate have returned to normal and the child is again alert, interested in his environment and gaining in weight. At that time a very gradual return to normal activity, under close supervision, should be instituted.

Coburn[5] and Taran[20, 21] have expressed the belief that massive doses of salicylates given early in the exudative phase change the course of the disease. This view has not been generally accepted. Murphy,[13] in a histological study of the exudative lesions in patients with acute rheumatic fever receiving large doses of salicylates, found no evidence to support the contention that salicylates exert a specific effect on the underlying disease process. The value of salicylates in the symptomatic therapy of the exudative phase is universally recognized. Salicylate therapy should be discontinued for at least two weeks, with a reevaluation of the patient at the end of that time, before any other changes in therapy are made, for salicylates not only suppress the acute symptoms but alter laboratory findings.

The controversy over the use of digitalis continues. Pediatric cardiologists are extremely cautious in use of the drug. The toxic and the therapeutic dose are very close, and Taran[21] has expressed the belief that, in active rheumatic fever, the toxic dose is less than the therapeutic dose. The drug may be of some value as a last resort in the patient with right-sided heart failure, but the results are not encouraging. The digitalizing dose is 100 mg. per 10 pounds of body weight, given in divided doses at intervals of six hours. The maintenance dose is 10 mg. per 10 pounds.

The dose of the more rapidly acting digitoxin is 0.1 mg. per 10 pounds of body weight, with a maintenance dose of 0.01 mg. per 10 pounds. Digifolin® is given intramuscularly in a digitalizing dose of 20 to 60 mg. per 10 pounds of body weight, with a maintenance dose of 2 to 6 mg. per 10 pounds.

The mercurial diuretics have been recommended by Taran[20, 21] for the treatment of congestive heart failure. The diuretic is given until a dry or stabilized weight is obtained, at which time the patient is put on a maintenance dose. This may be continued for months or years.

The use of continuous oxygen to promote cardiac rest and to reestablish the normal relation between systole and diastole has been urged by Taran.[20, 21] This increases cardiac output and improves the general condition and well-being of the patient.

The indications for tonsillectomy for the child with rheumatic fever are no different than for the non-rheumatic child. If the tonsils are unduly large or diseased and the child is subject to recurrent otitis media, cervical adenitis and nasal obstruction, the tonsils and adenoids should be removed. The operation should not be performed, however, until all signs of rheumatic activity have disappeared, since recrudescences may result from operation while the disease is active. Carious teeth or abscessed roots may be foci of infections and contribute to the continuation of the active phase of the disease. All infected teeth should be repaired during the inactive phase.

When any surgical or other procedures which might possibly spread a localized infection are contemplated a sulfonamide drug or penicillin should be given prophylactically preoperatively and for a week postoperatively.

SULFONAMIDES

The value of the sulfonamides in preventing recurrences of rheumatic fever has been amply demonstrated and reviewed by Hansen.[7] It has been estimated that a child who is receiving a sulfonamide continuously is only one-tenth as liable to have recurrence as the child who is not. The dose is 1.0 gm. of sulfadiazine or sulfamerazine a day, and it should be continued for a minimum of five years, but preferably through puberty regardless of length of time. The patient should be examined for signs of intoxication at weekly intervals for the first six weeks and at six-week intervals thereafter.

Massell and co-workers[11] in a study of oral administration of penicillin in patients with rheumatic fever found that 100,000 to 200,000 units of penicillin three times a day completely eradicated hemolytic streptococci from the throats of 75 per cent. Even in those patients in whom the organisms were not completely eradicated, they were greatly suppressed so that streptococci were not shown on cultures during the period penicillin was administered. The authors felt that this indirect evidence indicated penicillin might be practicable for the prevention of hemolytic streptococci and hence for rheumatic fever prophylaxis.

Prompt sulfonamide therapy of streptococcic infections among rheumatic susceptible patients will not prevent rheumatic recurrences. Rantz and coworkers[14] expressed the belief that prompt penicillin therapy of streptococcal infections interferes with the immune response by eliminating streptococci from the throat before toxins can be produced and disseminated in an appreciable quantity. It may be possible by prompt penicillin therapy of the streptococcal infection to prevent the chain of events which result in the rheumatic state.

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